BIOGRAPHICAL SKETCH

NAME Paul Yaswen	POSITION TITLE Staff Scientist
eRA COMMONS USER NAME P_Yaswen	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Tufts U., Medford, MA	B.Sc.	05/80	Biology
Brown U. Providence, RI	Ph.D.	12/84	Cell & Mol. Biology
Dana-Farber Cancer Institute Boston, MA	Postdoc	07/88	Cancer Genetics

A. Personal Statement

The main objective in my laboratory is to understand the molecular defects (both genetic and epigenetic) that contribute to malignancy of human epithelial cells. I have over 25 years of experience using tractable human mammary epithelial cell culture systems to model processes involved in immortal and malignant transformation of this cell type, the precursor of most human breast cancers. My group is widely recognized for work on the molecular mechanisms that limit the proliferative potential of human breast cells. In addition, we have successfully elucidated the regulation and function of the *ZNF217* oncogene, and defined factors involved in regulation of the *hTERT* gene - encoding the catalytic subunit of telomerase. In recent studies supported by an NIEHS/NCI sponsored Breast Cancer and the Environment Research Center and NASA, we have used cultured primary human breast cells to study the effects of radiation - a prototypical carcinogen, on the regulation of epithelial cell self-renewal and differentiation. Our published work indicates that limits, including those imposed by the tumor suppressor protein $p16^{INK4A}$, on the proliferative potential of normal cells may be consequences of pathways that exist to suppress tumorigenicity. However, these same senescence pathways may also contribute to aging by limiting the self-renewal capacity of normal stem/progenitor cells. I am currently an affiliated member of the Berkeley Stem Cell Center, and a preceptor in an NIH funded Biology of Aging Training Program jointly administered by LBNL and the Buck Institute. I have mentored 25 post-docs since 1993, many of who have gone on to successful careers in academia and industry.

B. Positions and Honors

Professional Experience

1981-1982 Graduate Teaching Assistant, Division of Biology and Medicine, Brown University
1985-1987 Research Fellow, Dept. of Cancer Genetics, Dana-Farber Cancer Inst., Harvard Medical School
1987-1988 NRSA Fellow, Dept. of Cancer Genetics, Dana-Farber Cancer Institute, Harvard Medical School
1988-1990 NRSA Fellow, Dept. of Cell and Molecular Biology, Lawrence Berkeley National Laboratory, University of California
1990-present Staff Scientist, Life Sciences Division, Lawrence Berkeley National Laboratory, University of California
1998-2009 Member, UCSF Comprehensive Cancer Center

Professional Service

1996-1999 Instructor – National Breast Cancer Coalition Project LEAD
2001 Ad hoc member, Pathology C Study Section, NIH, Center for Scientific Review
2002 Ad hoc member, Cancer Mol. Pathobiology Study Section, NIH, Center for Scientific Review
2004 Co-Chair - Senescence & Immortalization Minisymposium, AACR Ann. Mtg. Orlando, FL
2005-2009 Ad hoc member, Molecular Oncology Study Section, NIH, Center for Scientific Review

Awards:

1980, University Fellowship, Brown University; 1983, NIH Predoctoral Traineeship; 1987, NRSA Postdoctoral Fellowship; 2011, Honor Thy Healer Award for Community Breast Cancer Research, Zero Breast Cancer

C. Selected Peer-reviewed Publications (from 71 total)

Most relevant to the current application

1. Bazarov, A.V, Lee, W.J., Bazarov, I., Bosire, M., Hines, W.C., Stankovich, B., Chicas, A., Lowe, S.W., and **Yaswen, P**. The specific role of pRb in p16INK4A mediated arrest of normal and malignant human breast cells. Cell Cycle 11:1008-1013, 2012. PMCID:PMID22333593
2. Horiuchi, D., Kusdra, L., Huskey, N.E., Chandriani, S., Lenburg, M.E., Gonzalez-Angulo, A.M., Creasman, K.J., Bazarov, A.V., Smyth, J.W., Davis, S.E., **Yaswen, P**., Mills, G.B., Esserman, L.J., Goga, A. MYC pathway activation in triple-negative breast cancer is synthetic lethal with CDK inhibition. J Exp Med. 209:679-96, 2012. PMCID: PMC22430491
3. Mukhopadhyay, R., Costes, S., Bazarov, A., Hines, W.C., Barcellos-Hoff, M.H., and **Yaswen, P**. Promotion of variant human mammary epithelial cell outgrowth by ionizing radiation: an agent-based model supported by in vitro studies. Breast Cancer Res. 12:R11, 2010. PMCID: PMC2880432.
4. Bazarov, A.V., Hines, W.C., Lee, L., Bassett, E., Beliveau, A., Campeau, E., Mukhopadhyay, R., Lee, W.J., Melodyev, S., Zaslavsky, Y., Rodier, F., Benhattar, J., Ren, B., Campisi, J., and **Yaswen, P**. $p16^{INK4A}$ mediated suppression of telomerase in normal and malignant human breast cells. Aging Cell: 9:736-46, 2010. PMCID: PMC2941554.
5. Beliveau, A., Mott, J.D., Lo, A., Chen, E.I., Koller, A.A., **Yaswen, P**., Kenny, P.A., Muschler, J., and Bissell, M.J. Level of MMP-9 expression regulates maintenance or loss of tissue polarity in non-malignant and malignant breast cells in three-dimensional laminin-rich extracellular matrix. Genes & Dev. 24:2800-11, 2010. PMCID: PMC21159820.
6. Fournier, M.V., Fata, J., Martin, K., **Yaswen, P**., and Bissell, M.J. Interaction of E-cadherin and PTEN regulates morphogenesis and growth arrest in human mammary epithelial cells. Cancer Res. 69:4545-52, 2009. PMCID: PMC2746025.
7. Beliveau, A., Bassett, E., Lo, A.T., Garbe, J., Rubio, M.A., Bissell, M.J., Campisi, J., and **Yaswen, P**. p53-dependent integration of telomere and growth factor deprivation signals. Proc. Nat. Acad. Sci. (USA), 104:4431-6, 2007.
8. **Yaswen, P**. and Campisi, J. Oncogene-induced senescence pathways weave an intricate tapestry. Cell 128:233-4, 2007.
9. Fournier, M., Martin, K.J., Xhaja, K., Bosch, I., **Yaswen, P**., and Bissell, M.J., Gene expression signature in organized and growth arrested mammary acini predicts good outcome in breast cancer. Cancer Res. 66:7095-102, 2006. PMCID: PMC2933218.

Additional recent publications of importance to the field (in chronological order)

1. Nguyen-Ngoca, K-V., Cheung, K.J., Brenot, A., Shamira, E.R., Gray, R.S., Hines, W.C., **Yaswen, P.**, Werb, Z., and Ewald, A.J. The ECM microenvironment regulates collective migration and local dissemination in normal and malignant mammary epithelium. Proc. Nat. Acad. Sci. (USA), 109:E2595-604, 2012.
2. Pirone, J.R., D'arcy, M., Stewart, D.A., Hines, W.C., Johnson, M., Gould, M.N., **Yaswen, P.**, Jerry, D.J., Schneider, S.S., and Troester, M.A. Age-associated gene expression in normal breast tissue mirrors qualitative age-at-incidence patterns for breast cancer. Cancer Epidemiol. Biomarkers Prev., 21:1735-44, 2012, 2012.
3. Littlepage, L.E., Adler, A.S., Kouros-Mehr, H., Huang, G., Chou, J., Krig, S.R., Griffith, O.L., Korkola, J.E., Qu, K., Lawson, D.A., Xue, Q., Sternlicht, M.D., Dijkgraaf, G.J., **Yaswen, P.**, Rugo, H.S., Sweeney, C.A., Collins, C.C., Gray, J.W., Chang, H.Y., and Werb, Z. The transcription factor ZNF217 is a prognostic biomarker and therapeutic target during breast cancer progression. Cancer Discov. 2:638-51, 2012.
4. Krig, S.R., Jin, V.X., Bieda, M.C., O'geen, H., **Yaswen, P**., Green, R., and Farnham, P.J. Identification of genes directly regulated by the oncogene ZNF217 using ChIP-chip assays. J. Biol. Chem. 282:9703-12, 2007.

5. Chin, K., Ortiz de Solorzano, C., Knowles, D., Jones, A., Chou, W., Garcia Rodriguez, E., Kuo, W-L. Ljung, B-M., Chew, K., Garbe, J., Myambo, K., Krig, S., Stampfer, M., **Yaswen, P**., Gray, J.W., and Lockett, S.J. *In situ* analyses of genome instability in breast cancer. Nature Gen. 36: 984-988, 2004.
6. Beauséjour, C.M., Krtolica, A., Galimi, F., Narita, M., Lowe, S.W., **Yaswen, P**. and Campisi, J. Reversibility of human cellular senescence: Roles of the p53 and p16 pathways. EMBO J. 22: 4212-4222, 2003.
7. Stampfer, M.R., Garbe, J., Nijjar, T., Wigington, D., Swisshelm, K., and **Yaswen, P**. Loss of p53 function accelerates acquisition of telomerase activity in indefinite lifespan human mammary epithelial cell lines. Oncogene, 22: 5238-5251, 2003.
8. Olsen, C.L., Gardie, B., **Yaswen, P**., and Stampfer, M.R. Raf-1-induced growth arrest in human mammary epithelial cells is p16-independent and is overcome in immortal cells during conversion. Oncogene 21: 6328 – 6339, 2002.
9. **Yaswen, P**. and Stampfer, M.R. Molecular changes accompanying senescence and immortalization of cultured human mammary epithelial cells. Int. J. Biochem. Cell Biol. 34: 1382–1394, 2002.
10. Nonet, G.H., Stampfer, M.R., Chin, K., Gray, J.W., Collins, C.C., and **Yaswen, P**. The *ZNF217* Gene amplified in breast cancers promotes immortalization of human mammary epithelial cells. Cancer Res. 61: 1250-1254, 2001.
11. Stampfer, M.R., Garbe, J., Levine, G., Lichtsteiner, S., Vasserot, A.P., and **Yaswen, P**. hTERT expression can induce resistance to TGFβ growth inhibition in $p16^{INK4A}$(-) human mammary epithelial cells. Proc. Nat. Acad. Sci. (USA), 98: 4498-4503, 2001.

D. Research Support

ONGOING

U01 ES019458 (Werb/Yaswen) 09/01/10 – 04/30/15
National Institute of Environmental Health Sciences Subcontract to LBNL from UCSF
Environmental Effect on the Mammary Gland across the Lifespan
The intent of this project is to use human breast cells to develop a tissue specific risk model representing two major processes in carcinogenesis. While it is not currently possible to simulate oncogenic progression in its entirety using human cells, aberrant differentiation and self-renewal are important surrogate endpoints that can be used directly in estimates of cancer risk.

17UB-8708 (Vulpe/Yaswen) 08/01/11 – 05/31/14
California Breast Cancer Research Program
Building on National Initiatives for New Chemicals Screening
We will adapt cell-based tests used by EPA to make them relevant to breast cancer by transferring the methods into breast cells. We will also develop new tests to fill gaps in current testing methods, for example tests that measure changes in mammary-cell specific enzymes involved in estrogen production. By comparing the effects of chemicals that we know cause tumors in animal studies (carcinogens) to those chemicals that do not (non-carcinogens), we will be able to identify a set of tests that can help predict which chemicals might raise the risk of the disease.

RECENTLY COMPLETED

NNA10DE03I (Yaswen) 03/01/10 – 02/28/13
National Aeronautics and Space Administration
Epigenetic effects of radiation on epithelial cell self-renewal
Using a three-dimensional cell culture system that supports tissue-like behavior of human breast cells, we will: 1) determine the effects of ionization density and dose on the frequency of self-renewal versus differentiation, 2) identify biochemical pathways that show persistent changes as functions of ionization density and dose, and 3) use genetic manipulations to test the mechanistic involvement of discrete pathway components in persistent radiation quality effects.